OFFICE OF NAVAL RESEARCH

FINAL TECHNICAL REPORT

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CONTRACTOR: The Research Foundation of the State University of New York, Albany, N.Y.

WORK DONE AT: School of Medicine, State University of New York at Buffalo, Buffalo, N.Y.

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PROJECT TITLE: NEUROLOGIC ASPECTS OF HIGH BAROMETRIC PRESSURE PHENOMENA AND THE EFFECT OF ATMOSPHERIC CONTAMINANTS UPON NERVOUS SYSTEM ACTIVITY.

DATE: 15 April 1965

Contract Nonr 4343(00) was a continuation contract of Nonr 969(04) (see Final Technical Report Nonr 969(04), dated 31 December 1964, and Annual Report Nonr 4343(00) dated 1 May 1965.)

The Objectives and Aims of the project were not changed from those previously described. The work accomplished was limited by personnel problems (high turnover, illness) and the necessity of moving the laboratory facilities several miles.

SUMMARY OF RESULTS:

I. Carbon Dioxide Experiments. Further biochemical studies have demonstrated that changes in concentrations of electrolytes previously observed in cerebral cortex and mixed-venous plasma during and after exposure to 35% carbon dioxide - 65% oxygen are paralleled by changes in skeletal and cardiac muscle electrolyte concentrations (Table I.) The muscle electrolyte changes have been calculated as probably sufficient to account for the redistribution of electrolytes during the exposures, but the lack of data from liver analysis limits the conclusions that may be drawn.

Changes in carbon dioxide and phosphorus content of plasma and cerebral cortex have been determined during and after exposures to carbon dioxide (Table II.) Data are not complete, nor were all analyses completed before the project was terminated. Preliminary inspection of the data suggests that non-convulsive exposures to carbon dioxide produce significant changes in plasma inorganic phosphorus and possibly a change in the distribution of phosphorus between the high-energy bonds and the inorganic pool. This may reflect changes in basic oxidative-phosphorylation at some point

within the cerebral cortex-plasma system, as yet undetermined. Liver and muscle analyses have not yet been done.

New studies were begun on the relationship between age and previous exposure experience to the changes in respiratory rates of rats exposed to mixtures of carbon dioxide and oxygen, and carbon dioxide, oxygen, and nitrogen. Whole litters of rats were obtained as newborns from the breeding colony and isolated to prevent excessive pulmonary infections. Litters were exposed at weekly intervals to CO2-O2 (35/65) or CO2-O2-N2 (35/20/45) mixtures randomly. Respiratory rates were counted per animal at two to three minute intervals during the exposure and during the first two minutes of recovery on air. Preliminary inspection suggests a difference between the response to the two gas mixtures when animals were separated into two groups on the basis of weight. The weight division was made at 195 grams. The exposure series will continue until about 15 May 1965, a period of 120 days, to test for evidence of tolerence or the development of adaptation (supported by funds from independant sources.)

II. Oxygen Exposures. Analysis of accumulated data has continued. Studies were initiated, but not completed on the influence of varying inert gases on the incidence of oxygen convlusions, no conclusions can be made with data available. Studies were initiated on the effect of body temperature on oxygen convlusions, and collateraly on the effect of water immersion with changes in body temperature on oxygen convulsions. Insufficient data were collected before project termination for analysis. (A proposal for a new program at the Indiana University Medical Center will include these studies.)

A review of our data has revealed that 650 rats were exposed to hyperbaric oxygen, and of these 230 were exposed more than one time. No paralytic complications from these exposures have been observed.

Several tests were done using the 400 atmosphere chamber to determine the feasibility of specific studies. Eight rats have been exposed to pressures as high as 150 atmospheres, two died during the exposure, and two died within one hour of surfacing. Decompression schedules were calculated according to ideas obtained from CDR Robert Workman, EDU. The complete lack of visual monitering hinders the experiments. Electrophysiologic monitoring was done through a television camera cable. The EEG, EKG, ventilatory rate, body temperature, and total body movement were recorded from the animals. Chamber temperature, oxygen partial pressure, and carbon dioxide partial pressure were measured at intervals. Visual monitoring is sorely needed, and discussions have been initiated with the Fiber optics section of Bausch and Lomb, Rochester, N.Y., on the design of an appropriate system.

Last year, (see Final Technical Report 969(04)) studies were done contrasting the effects of pre-treatment of rats with Tris buffer or with acetazolamide on the occurrence and latency of oxygen convulsions. Parallel experiments were conducted with matched body-weight animals that were injected with Normal Saline, 0.3 Molar Tris buffer, and acetazolemide intra-peritoneally. They were sacrificed on a schedule comparable to the time of group HOP seizures (mean time) and plasma and cerebral cortex samples were obtained.

Plasma pH and total carbon dioxide, and cerebral cortex total carbon dioxide were determined. (Table III.) Saline was used as an isotonic (albeit not iso-osmotic) control against the large volume of Tris buffer. The small volume of acetazolamide did not appear to require a fluid volume control (less than 0.3 cc per injection).

The cerebral cortex carbon dioxide was elevated significantly under all experimental conditions. Both saline and Tris buffer caused non-significant elevations of the plasma carbon dioxide content. Acetazolamide (a carbonic anhydrase inhibitor) in two hours decreased the plasma carbon dioxide content, and increased the cerebral cortex carbon dioxide without a significant shift in plasma hydrogen ion concentration. After three hours the above changes are greater, and the hydrogen ion concentration had significantly increased. The data collection times were selected for oxygen exposures on the basis of reports in the literature that alterations in cerebral blood flow and intracranial pressure that follow the administration of acetazolamide have disappeared when the enzyme inhibitor is administered by this route. Further studies are obviously indicated regarding this problem, especially of the fate of other electrolytes.

PUBLICATIONS AND REPORTS DURING THIS CONTRACT

1. Neurologic hazards of diving. Technical Report No. 64-1. A.M.A. Arch. Environ. Health. In Press.

2. (with P. T. Hsu Cheng) Electrolyte changes in plasma and cerebral cortex from carbon dioxide exposures. Technical Report No. 64-2. To be published.

3. (with P. T. Hsu Cheng) Changes in distribution of cerebral cortex carbon dioxide during and after exposure to carbon dioxide. Technical Report 64-3 . To be published.

4. Seizure Initiation Mechanisms: Effects of carbon dioxide and oxygen. Presented at the American Epilepsy Society, December 1964, New York City. Technical Report No. 65-1 . To be published.

As mentioned in the Annual Report of this Contract dated 1 May 1964 continued availability of space was undetermined from March 1964 through August 1964. In September 1964 the School of Medicine made available space in the Public Health Research Institute. A request for a no-cost-to-the-government extension of the contract was submitted, and was finally approved three weeks before the closure date requested in the extension. By this time the Principal Investigator was no longer able to carry the payroll personally and technicians and associates had obtained other positions.

It is regretted that such problems did occur and that much of the tissue analyses are not yet completed. The Principal Investigator is moving to the Indiana University Medical Center in June 1965, and it is hoped that a new program can be initiated to permit completion of the programs contained in this and preceeding Contracts.

Table I

Tissue Material		Exposure Times							
		Control	5min,	7min,	10min,	15min,	30min,	Rec 30,	Rec 60
Thigh muscle	Potassium	110	113*	113	113	114	114	110	110
	Sodium	20	19+	19	18	18	18	19	19
Heart muscle	Potassium	70	72	72	72	72	72	69+	69
	Sodium	33	34	34	34	34	34	33	33

(all values reported as mEq/ kilo wet tissue)

Table II

Tissue Material		Exposure Time								
		Control	5min,	7min,	10min,	15min,	30min,	Rec 30,	Rec 60,	
Cerebral cortex	total CO2	12	20*	20	20	21	23	15*	14*	mM/Kg wet
	total P	2.9	3.0	3.0	3.0	3.0	3.0	3.0	3.0	Gm/Kg wet
Plasma	inorg P	7.9	9.75*			14.3*	15.4	9.6*		

* - p, less than 0.01 means difference from control and preceding value (data)

+ - p, less than 0.05 means difference from control and/or preceding value (data)

Table III

Type Treatment		Plasma	Cerebral Cortex	Dose-route
	pH	Total CO2 mM/L	Total CO2 mM/Kg wet	all IP
Control	7.31	22.58	12.63	
Saline 0.9%	7.33	24.59	15.38*	same volume as Tris
Tris 0.3M	7.31	24.80	16.37*	10mM/Kg
Diamox - 2hr	7.31	21.49*	16.81*	20mg./Kg
Diamox - 3hr	7.17*	20.68*	16.92*	

* -p, less than 0.01 means difference from control